IN THE SPECIFICATION

Please amend paragraph [0031] as follows:

[0031] By saying that an endonuclease cuts "beyond" the 3' end of a hairpin nucleic acid means that the cleavage site of the endonuclease cleaves at a point beyond the 3' end of the hairpin, between nucleotides that have been added to the hairpin. For instance, if a hairpin nucleic acid ends in the sequence . . . GAGTC-3', and has a strand attached to it that begins with 5'-AATTGGCC . . . , then the endonuclease N.BstNBI will cut between T and G of the attached strand, that is, at GAGTC AATT GGCC (SEQ ID NO: 3).

Please amend paragraphs [0055]-[0057] as follows:

[0055] FIG. 3 is a diagram showing a hairpin containing a nicking site of the nicking endonuclease N.BstNBI. The sequences shown therein, in 5' to 3' order, are NNNNNNNNNGACTC (SEQ ID NO: 1) and GAGTCNNNNNNNNN 3' (SEQ ID NO: 2).

[0056] FIG. 4 is a diagram showing a hairpin containing a cleavage site of blunt end endonuclease MlyI. The sequences shown therein, in 5' to 3' order, are NNNNNNNNNGACTC (SEQ ID NO: 1) and GAGTCNNNNNNNNN 3' (SEQ ID NO: 2).

[0057] FIG. 5 is a diagram showing a double-stranded nucleic acid anchor containing a nicking site of the nicking endonuclease N.BstNBI. The sequences shown therein, in 5' to 3' order, are NNNNNNNNNGACTC (SEQ ID NO: 1) and GAGTCNNNNNNNNN 3' (SEQ ID NO: 2).

Please amend paragraph [0074] as follows:

[0074] Several enzymes are known to nick DNA in a single strand but most are found in multiple protein complexes involved in DNA replication or in DNA repair, and as such, have before now had limited applications in manipulating DNA in vitro. However, a number of these enzymes are commercially available and can be used to nick DNA under simple reaction conditions. For example, N.BstNBI (available from New England Biolabs, Beverly, Mass., USA) has been used to prepare substrates for studies into DNA repair mechanisms. This and other such enzymes are shown in Table 1, below. A number are available commercially (e.g., N.AlwI, N.BstNBI, N.BbvCIA and N.BbvCIB are available from New England BioLabs, Inc., Beverly, Mass., USA). Information on enzymes and their cleavage sites can be found in the relevant scientific literature, and/or in public databases, e.g., REBASE (Robert et al., 2001, Nucl. Acids Res. 29:268-269) ("rebase/"), which is maintained by New England Biolabs on its web site ("neb.com"). The restriction site for N.MlyI, as listed in Table 1, is GAGTCNNNNN (SEQ ID NO: 4).

Please amend paragraph [0076] as follows:

[0076] N.BstNBI recognizes the asymmetric sequence GAGTC ~~(SEQ ID NO:1)~~ in double stranded DNA and nicks between the fourth and fifth base downstream of this sequence in the same strand. As described herein, this restriction site has been incorporated into the 3' end of DNA hairpins such that the N.BstNBI enzyme nicks the hairpin just upstream of the synthetic complementary strand, thereby detaching it from the hairpin.

Please amend paragraph [0079] as follows:

[0079] "Blunt end endonucleases" are those which hydrolyze both strands of a nucleic acid, and do so without leaving an overhanging end. A number of blunt end endonucleases are listed in Table 2, below. The restriction sites for some of the blunt end endonucleases listed in Table 2 are accorded sequence identifiers as follows: MlyI is GAGTCNNNNN (SEQ ID NO: 4); MslI is CAYNNNNRTG (SEQ ID NO: 5); OliI is CACNNNNGTG (SEQ ID NO: 6); PshAI is

GACNNNNGTC (SEQ ID NO: 7); SspD5I is GGTGANNNNNNNN (SEQ ID NO: 8); and XmnI is GAANNNNTTC (SEQ ID NO: 9).

Please amend paragraphs [0085]-[0091] as follows:

[0085] The MlyI restriction site can be "added" to the above sequence by merely adding an extra nucleotide:

5'-NNNNNGACTC . . . GAGTCNNNNN-3'.

The sequences shown above are accorded the following sequence identifiers: NNNNNGACTC (SEQ ID NO: 10) and GAGTCNNNNN-3' (SEQ ID NO: 4).

[0086] This sequence would form the hairpin:

```
                2
[CTCAGNNNN  N▼-5'
[GAGTCNNNN▲N▲-3'
          1 2
```

where, when the sequence has formed a hairpin, the arrow "1" indicates the site of the nick made by N.BstNBI, and the arrow "2" indicates the site on each "strand" that is cut by MlyI. The sequences shown in the above hairpin, in 5' to 3' order, are NNNNNGACTC (SEQ ID NO: 10) and GAGTCNNNNN 3' (SEQ ID NO: 4).

[0087] One can also make use of enzymes that do not recognize the same site. For instance, the blunt end endonuclease SspD5I recognizes the sequence 5'-GGTGANNNNNNNN^ -3' (SEQ ID NO: 8); [.] this site can be added into the hairpin shown above by overlapping the end of the SspD5I site with the N.BstNBI and MlyI sites:

where the arrow "1" indicates the site of the nick made by N.BstNBI, and the arrow "2,3" indicates the site on each "strand" that is cut by either MlyI or SspD5I. The sequences shown in the above hairpin, in 5' to 3' order, are NNNNNTACTCACC (SEQ ID NO: 11) and GGTGAGTCNNNNN 3' (SEQ ID NO: 12).

[0088] There is no requirement that the cleavage sites of one or more of the enzyme be in common, and a number of different sites can be incorporated into the same sequence. For instance, the following sequence

has a nicking site for N.BstNBI (restriction site GAGTCNNNN^) at the arrow "1", a cleavage site for the blunt cutter MlyI (restriction site GAGTCNNNNN^; SEQ ID NO: 4) at arrow "2", a cleavage site for the blunt cutter Hpy8I (restriction site GTN^NAC) at arrow "3", and a nicking site at arrow "4" for N.CviII (restriction site C^CD). Thus, a variety of restriction sites can be designed into the hairpin or anchor.

[0089] The hairpin can also be designed to have an overhang, that is, one "strand" can be longer than the other. This increases the number of possible restriction sites that can be designed into

the hairpin. For instance, the hairpin:

```
[CTCAGNACCGGT-5'
|GAGTCNTGG-3'
```

wherein the sequences shown in the above hairpin, in 5' to 3' order, are TGGCCANGACTC (SEQ ID NO: 13) and GAGTCNTGG.

[0090] can have a nucleic acid template added to its 5' end:

```
[CTCAGNACCGGTNNNN . . . -5'
|GAGTCNTGG          -3'.
```

The sequences shown in the above hairpin, in 5' to 3' order, are NNNNTGGCCANGACTC (SEQ ID NO: 14) and GAGTCNTGG.

[0091] Synthesis of the complementary strand will produce the following double-stranded nucleic acid:

```
                2  3
[CTCAGNACC  G▼GT▼NNNN . . . -5'
|GAGTCNTGG▲C▲CA▲NNNN . . . -3'
          1 2  3
```

which can be nicked at position 1 by N.BstNBI, and is cleavable across both strands at position 2 by MlyI, and at position 3 by BalI, another blunt cutter with restriction site TGG^CCA. The single stranded template can be removed by use of N.BstNBI, or the original hairpin can be recovered by using BalI, followed by N.BstNBI to recover the overhang. Alternatively, a new

type of blunt hairpin can be made by incorporating "CCA" onto the 3' end of the hairpin to make it completely double-stranded. The sequences shown in the above hairpin, in 5' to 3' order, are NNNNTGGCCANGACTC (SEQ ID NO: 14) and GAGTCNTGGNNNN (SEQ ID NO: 15).